Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	252	514/230.2; 544/89	USPAT	OR	OFF	2005/03/09 10:38

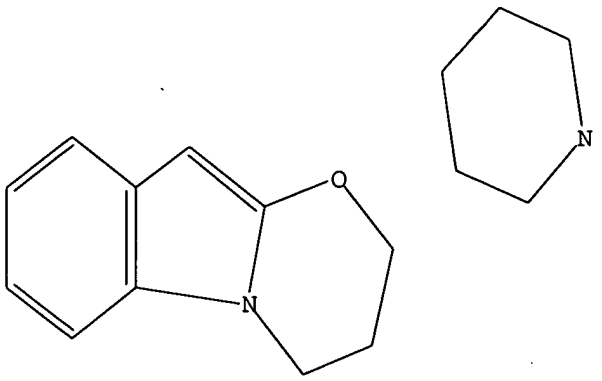
1 broad search

ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-13 7-8 8-13 8-9 9-10 10-11 11-12 12-13
14-19 14-15 15-16 16-17 17-18 18-19
exact/norm bonds :
6-13 8-13 8-9 9-10 10-11 11-12 12-13 14-19 14-15 15-16 16-17 17-18
18-19
exact bonds :
5-7 7-8
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 14 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 09:45:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 48 TO ITERATE

100.0% PROCESSED 48 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 545 TO 1375
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 09:45:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 966 TO ITERATE

100.0% PROCESSED 966 ITERATIONS 52 ANSWERS
SEARCH TIME: 00.00.01

L3 52 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.33	161.54

FILE 'CAPLUS' ENTERED AT 09:45:44 ON 09 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 9 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 8 Mar 2005 (20050308/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 33 L3

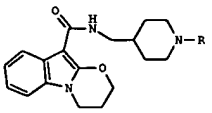
=> d ibib abs hitstr tot

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136569 CAPLUS
TITLE: Use of ZH-[1,3]oxazino[3,2-a]indole derivatives for the treatment of neuropathic pain
INVENTOR(S): Guglielmotti, Angelo; Polenzani, Lorenzo; Alisi, Alessandra; Cazzolla, Nicola
PATENT ASSIGNEE(S): Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Italy
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014001	A1	20050217	WO 2004-EP7633	20040708

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

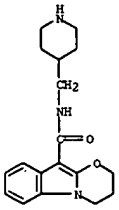
PRIORITY APPLN. INFO.: IT 2003-MI1467 A 20030718
GI



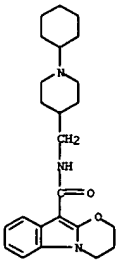
I

AB The invention discloses the use of I (R = H, linear or branched C1-12alkyl, arylalkyl), or an acid addition salt thereof with pharmaceutically acceptable organic or inorg. acids, to prepare a pharmaceutical composition for the treatment of neuropathic pain.
IT **152811-62-6 152811-89-7 152811-89-7D**, derivs.
841205-40-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxazinoindole derivs. for treatment of neuropathic pain)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

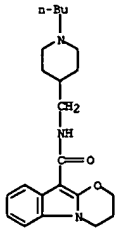


RN 841205-40-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

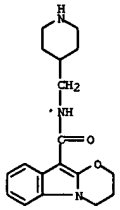


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1059201 CAPLUS
DOCUMENT NUMBER: 142:32977
TITLE: Pharmaceutical combinations of a proton pump inhibitor and a compound which modifies gastrointestinal motility
INVENTOR(S): Zimmermann, Peter Jan; Chiesa, M. Vittoria; Palmer, Andreas; Brehm, Christof; Klein, Thomas; Senn-Bilfinger, Joerg; Simon, Wolfgang-Alexander; Kromer, Wolfgang; Grundler, Gerhard; Hanauer, Guido; Buhr, Wilm; Postius, Stefan
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

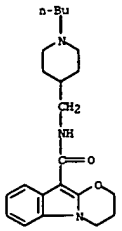
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105795	A1	20041209	WO 2004-EP50936	20040526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-11875 A 20030527
EP 2004-102304 A 20040525

AB The invention relates to the combination of certain active compds. from the acid pump antagonist class and compds. which modify gastrointestinal motility. The acid pump antagonist class is selected from a tricyclic imidazopyridine and the gastrointestinal motility modifier is selected from a 5-HT-(partial)-agonist/antagonist.
IT **152811-62-6**, Piboserod
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations of proton pump inhibitor and modifier of gastrointestinal motility)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

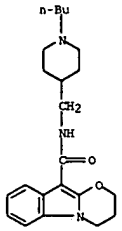
L4 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1011605 CAPLUS
DOCUMENT NUMBER: 142:127378
TITLE: The 5-HT4 receptor agonist, tegaserod, is a potent 5-HT2B receptor antagonist in vitro and in vivo
AUTHOR(S): Beattie, D. T.; Smith, J. A. M.; Marquess, D.; Vickery, R. G.; Armstrong, S. R.; Pulido-Rios, T.; McCullough, J. L.; Sandlund, C.; Richardson, C.; Mai, N.; Humphrey, P. P. A.
CORPORATE SOURCE: Theravance, Inc., South San Francisco, CA, 94080, USA
SOURCE: British Journal of Pharmacology (2004), 143(5), 549-560
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tegaserod (Zelnorm) is a potent 5-hydroxytryptamine4 (5-HT4) receptor agonist with clin. efficacy in disorders associated with reduced gastrointestinal motility and transit. The present study investigated the interaction of tegaserod with 5-HT2 receptors, and compared its potency in this respect to its 5-HT4 receptor agonist activity. Tegaserod had significant binding affinity for human recombinant 5-HT2A, 5-HT2B and 5-HT2C receptors (pKi = 7.5, 8.4 and 7.0, resp.). The 5-HT2B receptor-binding affinity of tegaserod was identical to that at human recombinant 5-HT4(c) receptors (mean pKi = 8.4) in human embryonic kidney-293 (HEK-293) cells stably transfected with the human 5-HT4(c) receptor. Tegaserod (0.1-3 μM) inhibited 5-HT-mediated contraction of the rat isolated stomach fundus potently (pA2 = 8.3), consistent with 5-HT2B receptor antagonist activity. Tegaserod produced, with similar potency, an elevation of adenosine 3',5' cyclic monophosphate in HEK-293 cells stably transfected with the human 5-HT4(c) receptor (mean pEC50 = 8.6), as well as 5-HT4 receptor-mediated relaxation of the rat isolated esophagus (mean pEC50 = 8.2) and contraction of the guinea-pig isolated colon (mean pEC50 = 8.3). Following s.c. administration, tegaserod (0.3 or 1 mg kg-1) inhibited contractions of the stomach fundus in anesthetized rats in response to i.v. dosing of α-Me 5-HT (0.03 mg kg-1) and BW 723C86 (0.3 mg kg-1), selective 5-HT2B receptor agonists. At similar doses, tegaserod (1 and 3 mg kg-1 s.c.) evoked a 5-HT4 receptor-mediated increase in colonic transit in conscious guinea-pigs. The data from this study indicate that tegaserod antagonizes 5-HT2B receptors at concns. similar to those that activate 5-HT4 receptors. It remains to be determined whether this 5-HT2B receptor antagonist activity of tegaserod contributes to its clin. profile.
IT 152811-62-6, Piboserod
RL: PAC (Pharmacological activity); BIOL (Biological study)
(5-HT4 receptor agonist, tegaserod, is a potent 5-HT2B receptor antagonist in vitro and in vivo)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

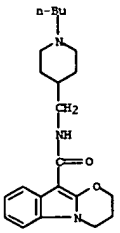
L4 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:647395 CAPLUS
DOCUMENT NUMBER: 141:254710
TITLE: G-protein coupled receptors: SAR analyses of neurotransmitters and antagonists
AUTHOR(S): Kuo, C. L.; Wang, R. B.; Shen, L. J.; Lien, L. L.; Lien, E. J.
CORPORATE SOURCE: School of Pharmacy, University of Southern California, Los Angeles, CA, USA
SOURCE: Journal of Clinical Pharmacy and Therapeutics (2004), 29(3), 279-298
CODEN: JCPTED; ISSN: 0269-4727
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: From the deductive point of view, neurotransmitter receptors can be divided into categories such as cholinergic (muscarinic, nicotinic), adrenergic (α- and β-), dopaminergic, serotoninergic (5-HT1.apprx.5-HT5), and histaminergic (H1 and H2). Selective agonists and antagonists of each receptor subtype can have specific useful therapeutic applications. For understanding the mol. mechanisms of action, an inductive method of anal. is useful. Objective: The aim of the present study is to examine the structure-activity relationships of agents acting on G-protein coupled receptors. Method: Representative sets of G-PCR agonists and antagonists were identified from the literature and Medline [P.M. Walsh (2003) Physicians' desk reference; M.J. O'Neil (2001) The Merck index). The mol. weight (MW), calculated logarithm of octanol/water partition coefficient (C log P) and molar refraction (CMR), dipole moment (DM), Elumo (the energy of the LUMO, a measure of the electron affinity of a mol. and its reactivity as an electrophile), Ehomo (the energy of the HOMO, related to the ionization potential of a mol., and its reactivity as a nucleophile), and the total number of hydrogen bonds (Hb) (donors and receptors), were chosen as mol. descriptors for SAR analyses. Results: The data suggest that not only do neurotransmitters share common structural features but their receptors belong to the same ensemble of G-protein coupled receptor with seven to eight transmembrane domains with their resultant dipoles in an antiparallel configuration. Moreover, the anal. indicates that the receptor exists in a dynamic equilibrium between the closed state and the open state. The energy needed to open the closed state is provided by the hydrolysis of GTP. A composite 3-D parameter frame setting of all the neurotransmitter agonists and antagonists are presented using MW, Hb and μ as independent variables. Conclusion: It appears that all neurotransmitters examined in this study operate by a similar mechanism with the G-protein coupled receptors.
IT 152811-62-6, Piboserod
RL: PRP (Properties)
(structure-activity relationship anal. of neurotransmitters and G protein-coupled receptor antagonists)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



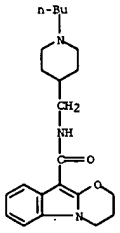
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:392318 CAPLUS
DOCUMENT NUMBER: 140:400077
TITLE: Pharmaceutical combinations including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and their use in treating gastrointestinal and abdominal visceral disorders
INVENTOR(S): Billstein, Stephan Anthony; Dumovic, Peter; Franco, Nicola; Iwicki, Mark Thomas; Pfannkuche, Hans-Jurgen; Wilusz, Edward Joseph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 722,784, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092511	A1	20040513	US 2003-702688	20031106
PRIORITY APPLN. INFO.:			US 1999-266333P	P 19991210
			US 2000-722784	B1 20001127

AB The invention discloses a combination of a first agent including either a 5-HT4 receptor agonist or antagonist or a 5-HT3 receptor antagonist and a co-agent and pharmaceutical compns. and formulations containing the combination. The invention also discloses a method for treating a gastrointestinal and abdominal visceral disorder by administering the pharmaceutical compns. to a patient. The pharmaceutical compns. may also be employed as laxatives, to prepare a patient for colonoscopy and to regulate and stabilize enterochromaffin cell secretory, pain and motility mechanisms, afferent fiber activity and GI and lower abdominal smooth muscle cells. The dosage is preferably oral and administration is preferably once or twice a day. The preferred first agent is tegaserod.
IT 152811-62-6, SB 207266
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of 5-HT4 agonist or antagonist or 5-HT3 antagonist and co-agent for treatment of gastrointestinal and abdominal visceral disorders)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

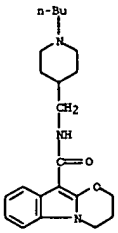


L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:931185 CAPLUS
DOCUMENT NUMBER: 140:744
TITLE: 5-HT4 receptor antagonists for the treatment of heart failure
INVENTOR(S): Levy, Finn Olav
PATENT ASSIGNEE(S): Medinnova SF, Norway; Dzieglewska, Hanna
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097065	A1	20031127	WO 2003-GB2134	20030516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1503764	A1	20050209	EP 2003-725415	20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			GB 2002-11230	A 20020516
			WO 2003-GB2134	W 20030516

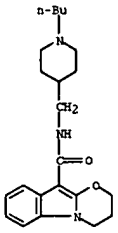
AB This invention provides the use of a 5-HT4 receptor antagonist in the manufacture of a medicament for treating or preventing heart failure. Particular heart disorders to be treated are selected from the group comprising chronic heart failure, congestive heart failure, chronic congestive heart failure and heart failure resulting from ischemic heart disease. Methods of treating heart failure using 5-HT4 receptor antagonists and pharmaceutical compns. containing 5-HT4 receptor antagonists are also provided. Treatment of post-infarction congestive heart failure in rats with 5-HT4 receptor antagonist SB207266 showed a trend towards normalization of myocardial function.
IT 178273-87-5, SB207266 hydrochloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT4 receptor antagonists for treatment of heart failure)
RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

IT 152811-62-6, SB207266
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as 5-HT4 antagonist; 5-HT4 receptor antagonists for treatment of heart failure)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



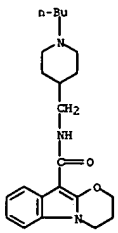
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:656546 CAPLUS
DOCUMENT NUMBER: 139:169361
TITLE: Pharmaceutical composition comprising piboserod or salt and process therefor comprising dry granulation
INVENTOR(S): Buxton, Philip Christopher; Groves, Sharon Elizabeth; Thomson, Seona; Van Schie, Dick Marinus Johannes; Yeates, Kenneth Trevor
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

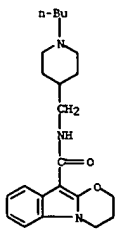
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068193	A1	20030821	WO 2003-GB217	20030122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1476136	A1	20041117	EP 2003-700915	20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007666	A	20050111	BR 2003-7666	20030122
PRIORITY APPLN. INFO.:			GB 2002-3526 A	20020214
			GB 2002-3528 A	20020214
			WO 2003-GB217 W	20030122

AB The invention provides a process for preparing a pharmaceutical composition comprising N-[1-nbutyl-(4-piperidinyl)methyl]-3,4-dihydro-ZH-[1,3]oxazino[3,2-a]indole-10-carboxamide (SB 207266) (piboserod) or a pharmaceutically acceptable salt thereof in combination with one or more pharmaceutically acceptable excipients, the process comprising forming part or all of the SB 207266 or the salt thereof into granules by a dry granulation process. The process is preferably a roller compaction process, preferably followed by milling to a suitable particle size. The granules are usually of increased particle size and/or compacted compared to the SB 207266 or the salt thereof. Preferably, the SB 207266 or the salt thereof is present in the composition and/or in the granules in at least 4
weight % and/or up to 60 weight % by weight of the composition and/or by weight of the
granules resp. An intragranular lubricant, filler (e.g. CaHPO4), and/or compression aid (e.g. microcryst. cellulose) are usually used. The invention also provides a pharmaceutical composition obtainable by the dry granulation process and/or which has been prepared by the dry granulation process.
IT 152811-62-6, PIboserod 152811-62-6D, Piboserod, salts

L4 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
178273-87-5, Piboserod hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. comprising piboserod or salt and process therefor comprising dry granulation)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

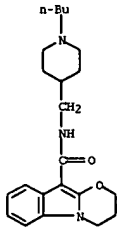


RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

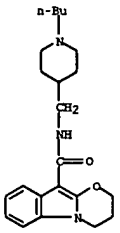


● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

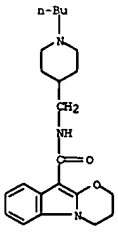
L4 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:295106 CAPLUS
DOCUMENT NUMBER: 139:301721
TITLE: Regulatory role of 5-HT and muscarinic receptor antagonists on the migrating myoelectric complex in rats
AUTHOR(S): Axelsson, Lars-Goran; Wallin, Berndt; Gillberg, Per-Goran; Sjoberg, Birger; Soderberg, Charlotte; Hellstrom, Per M.
CORPORATE SOURCE: Karolinska Institutet, Department of Internal Medicine, Section of Gastroenterology and Hepatology, Karolinska Hospital, Stockholm, SE-171 76, Swed.
SOURCE: European Journal of Pharmacology (2003), 467(1-3), 211-218
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-HT3 and 5-HT4 receptor antagonists alosetron and piboserod, and the muscarinic receptor antagonists PNU-171990A (2-(diisopropylamino)ethyl 1-phenylcyclopentanecarboxylate, hydrochloride) and PNU-174708A (2-(diisopropylamino)ethyl 1-phenylcyclohexanecarboxylate) were studied by electromyog., defining the migrating myoelec. complex (MMC) after i.v. administration in conscious rats. Alosetron prolonged the MMC cycle length from 16.6 to maximally 30.4 min at the dose 0.5 mg kg-1. Piboserod promptly abolished MMC pattern and prolonged cycle length from 16.5 to >60 min at 0.5 mg kg-1. PNU-171990A and PNU-174708A had no effect on basal cycle length up to a dose of 20 mg kg-1. In controls, saline did not change the MMC pattern, while l-hyoscyamine at the same dose, 20 mg kg-1, prolonged cycle length from 17.6 to 29.0 min. None of the drugs affected duration or propagation velocity of phase III of MMC. Blockade of 5-HT4 receptors seems to exert a powerful inhibitory effect on motility, 5-HT3 receptor blockade is less efficient and muscarinic receptor blockade has low efficacy.
IT 152811-62-6, Piboserod
RL: PAC (Pharmacological activity); BIOL (Biological study)
(regulatory role of 5-HT and muscarinic receptor antagonists on the migrating myoelec. complex in rats)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:452046 CAPLUS
DOCUMENT NUMBER: 137:163324
TITLE: Molecular Design Based on 3D-Pharmacophore. Application to 5-HT4 Receptor
AUTHOR(S): Bureau, Ronan; Daveu, Cyril; Lemaitre, Stephane; Dauphin, Francois; Landelle, Henriette; Lancelot, Jean-Charles; Rault, Sylvain
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Universite de Caen, Caen, 14032, Fr.
SOURCE: Journal of Chemical Information and Computer Sciences (2002), 42(4), 962-967
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A definition of a pharmacophore for the 5-HT4 antagonist was carried out by considering a three-dimensional model which correlates the chemical structures of series of antagonists with their biol. affinities. A mol. design is described by analyzing the differences between two 3D serotonin pharmacophores. This successful structural modification demonstrates the efficiency of this approach to design new serotonin ligands.
IT 152811-62-6
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(mol. design based on 3D-pharmacophore and application to 5-HT4 receptor)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:122823 CAPLUS
DOCUMENT NUMBER: 136:161371
TITLE: The use of 5HT4 receptor antagonists in the prophylaxis or treatment of certain cardiovascular conditions
INVENTOR(S): Bonhomme, Mireille Marguerite Jeanne; Bril, Antoine Michel Alain; Gout, Bernard Emile Joseph; Patel, Bela Rajiv; Shepherd, Gillian Louise
PATENT ASSIGNEE(S): Laboratoire Glaxosmithkline S.A.S., Fr.; Smithkline Beecham Corporation; Glaxo Group Limited
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011766	A2	20020214	WO 2001-GB3544	20010807
WO 2002011766	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2418904	AA	20020214	CA 2001-2418904	20010807
AU 2001076529	A5	20020218	AU 2001-76529	20010807
EP 1311295	A2	20030521	EP 2001-954184	20010807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004505930	T2	20040226	JP 2002-517100	20010807
BR 2001013073	A	20040622	BR 2001-13073	20010807
NZ 524108	A	20041126	NZ 2001-524108	20010807
NZ 535261	A	20041224	NZ 2001-535261	20010807
CA 2418921	AA	20020214	CA 2001-2418921	20010808
WO 2002011733	A1	20020214	WO 2001-GB3590	20010808
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DE, DK, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001076558	A5	20020218	AU 2001-76558	20010808
EP 1313481	A1	20030528	EP 2001-954214	20010808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013169	A	20030715	BR 2001-13169	20010808
JP 2004505920	T2	20040226	JP 2002-517069	20010808
AU 2002029161	A5	20020523	AU 2002-29161	20020327
AU 2002029162	A5	20020523	AU 2002-29162	20020327

L4 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

NO	2003000588	A	20030403	NO 2003-588	20030206
ZA	2003001031	A	20040420	ZA 2003-1031	20030206
ZA	2003003448	A	20040510	ZA 2003-3448	20030506
US	2005032866	A1	20050210	US 2003-344075	20030512
PRIORITY APPLN. INFO.:				GB 2000-19410	A 20000807
				GB 2000-19523	A 20000808
				GB 2000-19524	A 20000808
				GB 2001-18919	A 20010802
				GB 2001-19022	A 20010803
				AU 2001-76529	A3 20010807
				WO 2001-GB3544	W 20010807
				WO 2001-GB3590	W 20010808

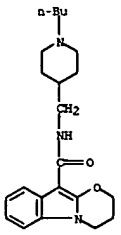
AB The invention relates to the use of a 5-HT4 receptor antagonist in the manufacture of a medicament for the prophylaxis or treatment of atrial remodelling in a mammal. Preferably, the antagonist is N-[(1.n-butyl-4-piperidinyl) methyl]-3,4-dihydro-ZH-[1,3]oxazino[3,2-a]indole-10-carboxamide (SB207266) or a pharmaceutically acceptable salt thereof. The invention also relates to the use of SB 207266 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment or prophylaxis of atrial fibrillation in a mammal by administering to the mammal a daily oral or parenteral dosage regimen of about 0.2 mg to 1.0 mg of the SB 207266 or salt thereof per kg of total body weight (measured as the free base). The invention also relates to the use of SB 207266 or a pharmaceutically acceptable salt thereof in the prophylaxis or treatment of atrial arrhythmia in a mammal by administration of the SB 207266 or salt thereof on the first day at a loading dose of about 1.2 to about 2.0 times the daily maintenance dose, followed by administration of the SB 207266 or salt at the daily maintenance dose on subsequent days.

IT 152811-62-6, SB207266
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of 5HT4 receptor antagonists in prophylaxis or treatment of certain cardiovascular conditions)

RN 152811-62-6 CAPLUS

CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

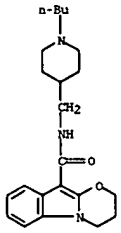
L4 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT 178273-87-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of 5HT4 receptor antagonists in prophylaxis or treatment of certain cardiovascular conditions)

RN 178273-87-5 CAPLUS

CN ZH-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:122795 CAPLUS

DOCUMENT NUMBER: 136:172790

TITLE: Pharmaceutical composition comprising condensed indole compound

INVENTOR(S): Buxton, Philip Christopher; Van Schie, Dirk Marinus Johannes; Thomson, Seona

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK; Laboratoire Glaxosmithkline S.A.S.

SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011733	A1	20020214	WO 2001-GB3590	20010808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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WO 2002011766	A2	20020214	WO 2001-GB3544	20010807
WO 2002011766	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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NZ 535261	A	20041224	NZ 2001-535261	20010807
CA 2418921	AA	20020214	CA 2001-2418921	20010808
AU 2001076558	A5	20020218	AU 2001-76558	20010808
EP 1313481	A1	20030528	EP 2001-954214	20010808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013169	A	20030715	BR 2001-13169	20010808
JP 2004505920	T2	20040226	JP 2002-517069	20010808
US 2003032640	A1	20030213	US 2002-55817	20020123
AU 2002029161	A5	20020523	AU 2002-29161	20020327
AU 2002029162	A5	20020523	AU 2002-29162	20020327
ZA 2003003448	A	20040510	ZA 2003-3448	20030506

PRIORITY APPLN. INFO.:

GB 2000-19524	A	20000808
GB 2001-18919	A	20010802
GB 2001-19022	A	20010803
WO 2001-GB3544	W	20010807
GB 2000-19410	A	20000807
GB 2000-19523	A	20000808
AU 2001-76529	A3	20010807
WO 2001-GB3590	W	20010808

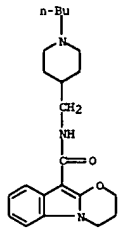
L4 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB A pharmaceutical composition comprising N-{1-[n-butyl-4-piperidinyl]methyl]-3,4-dihydro-ZH-[1,3]oxazino[3,2-a]indole-10-carboxamide (SB 207266) or a salt in combination with 1 or more carriers, wherein at least some of the SB 207266 or salt are in granulated form. Preferably, a filler and/or binder are also present. Thus, a tablet composition contained SB 207266 5.0, microcryst. cellulose 50.0, HPMC 12.5, sodium starch glycolate 12.5, dicalcium phosphate 1167.5, and Mg stearate 2.5 mg.

IT 152811-62-6, SB 207266 178273-87-5, SB 207266 hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising condensed indole compound)

RN 152811-62-6 CAPLUS

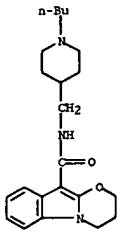
CN ZH-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 178273-87-5 CAPLUS

CN ZH-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

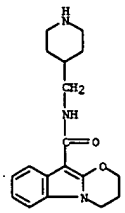
L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:591194 CAPLUS
DOCUMENT NUMBER: 135:344435
TITLE: Synthesis and pharmacological activity of metabolites of the 5-HT4 receptor antagonist SB-207266
AUTHOR(S): Fedouloff, M.; Hossner, F.; Voyle, M.; Ranson, J.; Powles, J.; Riley, G.; Sanger, G.
CORPORATE SOURCE: Department of Synthetic Chemistry, Smithkline Beecham Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(8), 2119-2128
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344435

AB Three metabolites of N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]-oxazino[3,2-a]indole-10-carboxamide (SB-207266) were synthesized and their pharmacol. activity determined

IT **152811-89-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and pharmacol. activity of metabolites of 5-HT4 receptor antagonist SB-207266)

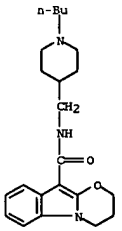
RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



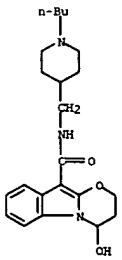
IT **152811-62-6P**, SB-207266, metabolites **227328-83-8P** **261787-90-0P** **371971-11-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of metabolites of 5-HT4 receptor antagonist SB-207266)

RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

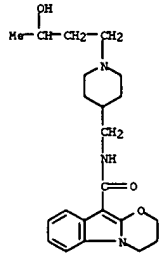


RN 227328-83-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-4-hydroxy- (9CI) (CA INDEX NAME)

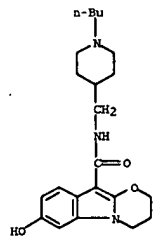


RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-hydroxybutyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



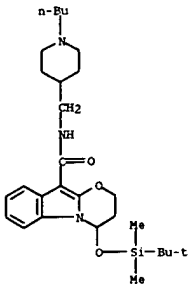
RN 371971-11-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-7-hydroxy- (9CI) (CA INDEX NAME)



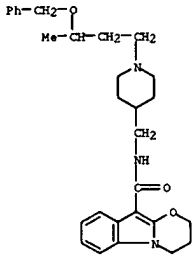
IT **227328-82-7P** **261787-98-8P** **371971-18-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and pharmacol. activity of metabolites of 5-HT4 receptor antagonist SB-207266)

RN 227328-82-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

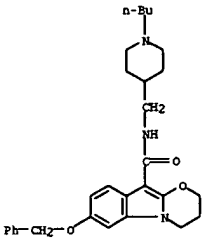


RN 261787-98-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-[3-(phenylmethoxy)butyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 371971-18-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

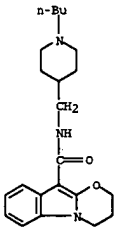
L4 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:286903 CAPLUS
DOCUMENT NUMBER: 135:204690
TITLE: Irritable bowel syndrome: New agents targeting serotonin receptor subtypes
AUTHOR(S): De Ponti, Fabrizio; Tonini, Marcello
CORPORATE SOURCE: Department of Pharmacology, University of Bologna, Bologna, Italy
SOURCE: Drugs (2001), 61(3), 317-332
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 138 refs. Although the past few years have seen an exponential growth of compds. of potential interest for the treatment of functional gastrointestinal (GI) tract disorders, the gap that still exists between basic and clin. research is easily noticed if one considers the relative paucity of drugs that have received marketing authorization for the treatment of irritable bowel syndrome (IBS). Traditional efficacy outcomes in drug development for IBS include the ability of the compound to affect GI tract motility (i.e. to exert a prokinetic or an antispasmodic effect), which is thought to be of importance if a motor disorder is the underlying pathophysiol. mechanism. More recently, altered visceral sensitivity to a distending stimulus has been suggested to be a key pathophysiol. feature, at least in some patients, and has become a target for therapeutic interventions. However, there is now growing consensus that the primary outcome measure in the treatment of functional disorders are those that reflect overall control of the patient's symptoms (pain, diarrhea, constipation) in everyday situations such as the clin. global improvement scales. Although, in general, guidelines on the design of treatment trials for functional GI tract disorders advise against subcategorization of patients according to the main symptom (because of symptom instability), subcategorization indeed makes sense especially in IBS (constipation- or diarrhea-predominant). Compds. with a specific indication for each subpopulation of patients are now emerging. The rationale for investigations on serotonin (5-hydroxytryptamine; 5-HT) receptor ligands in IBS rests mainly on the fact that serotonin, which may be released by enterochromaffin-like cells in the GI tract as well as from other sources, has a number of well documented motor effects on the GI tract and can produce hyperalgesia in several exptl. models. Serotonin receptors belonging to the 5-HT3 and 5-HT4 subtype are the most extensively studied in gastroenterol., although hitherto 'orphan' receptor subtypes, such as the 5-HT7 and the 5-HT1B/D receptors, are now emerging. Among 5-HT3 receptor antagonists, alosetron was recently approved for the treatment of diarrhea-predominant IBS and is an example of a compound that, at least theor., may act at multiple levels: by inhibiting visceral sensitivity, by increasing compliance, and by inhibiting excitatory 5-HT3 receptors located on both ascending and descending neuronal pathways involved in peristalsis. For this reason, 5-HT3 receptor antagonists may slow transit, hence the specific indication of alosetron in diarrhea-predominant IBS. However, alosetron has been recently withdrawn by the manufacturer because of safety concerns. Hypomotility remains an attractive therapeutic target in IBS and the new generation of prokinetics includes several partial agonists at the 5-HT4 receptor, such as tegaserod (HTF-919) and prucalopride (R0-93877). In addition, preliminary evidence suggests that 5-HT4 receptors may also be involved in the modulation of visceral sensitivity. Second-generation 5-HT4 receptor agonists seem to be devoid of the QT-prolonging effects observed in some clin. circumstances with cisapride and may be more active at the colonic level. Piboserod (SB-207266A) is a 5-HT4 receptor antagonist under development for the

L4 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

treatment of diarrhea-predominant IBS. Finally, interest in 5-HT7 and 5-HT1B/D receptor subtypes stems from the observation that the former receptors mediate smooth muscle relaxation (at least in the human colon), whereas sumatriptan (a 5-HT1B/D receptor agonist) can affect GI tract motility and visceral sensitivity.

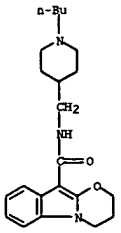
IT 152811-62-6, Piboserod
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of irritable bowel syndrome)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

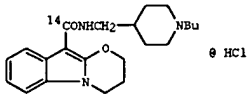
L4 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:840378 CAPLUS
DOCUMENT NUMBER: 134:110779
TITLE: Effects of a serotonin 5-HT4 receptor antagonist SB-207266 on gastrointestinal motor and sensory function in humans
AUTHOR(S): Bharucha, A. E.; Camilleri, M.; Haydock, S.; Ferber, I.; Burton, D.; Cooper, S.; Tompson, D.; Fitzpatrick, K.; Higgins, R.; Zinsmeister, A. R.
CORPORATE SOURCE: Gastroenterology Research Unit, Mayo Clinic and Mayo Foundation, Rochester, MN, 55905, USA
SOURCE: Gut (2000), 47(5), 667-674
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Serotonin 5-HT4 receptors are located on enteric cholinergic neurons and may regulate peristalsis. 5-HT4 receptors on primary afferent neurons have been postulated to modulate visceral sensation. While 5-HT4 agonists are used as prokinetic agents, the physiol. role of 5-HT4 receptors in the human gut is unknown. The authors' aim was to characterize the role of 5-HT4 receptors in regulating gastrointestinal motor and sensory function in healthy subjects under baseline and stimulated conditions with a 5-HT4 receptor antagonist. Part A compared the effects of placebo to four doses of a 5-HT4 receptor antagonist (SB-207266) on the cisapride mediated increase in plasma aldosterone (a 5-HT4 mediated response) and orocecal transit in 18 subjects. In part B, 52 healthy subjects received placebo, or 0.05, 0.5, or 5 mg of SB-207266 for 10-12 days; gastric, small bowel, and colonic transit were measured by scintigraphy on days 7-9, and fasting and postprandial colonic motor function, compliance, and sensation during distensions were assessed on day 12. Part A: 0.5 5, and 20 mg doses of SB-207266 had significant and quant. similar effects, antagonizing the cisapride mediated increase in plasma aldosterone and acceleration of orocecal transit. Part B: SB-207266 tended to delay colonic transit (geometric center of isotope at 24 (p=0.06) and 48 h (p=0.08)), but did not have dose related effects on transit, fasting or postprandial colonic motor activity, compliance, or sensation. 5-HT4 receptors are involved in the regulation of cisapride stimulated orocecal transit; SB 207266 tends to modulate colonic transit but not sensory functions or compliance in healthy human subjects.
IT 152811-62-6, SB-207266
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(SB-207266 efficacy as serotonin 5-HT4 receptor antagonist in humans)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



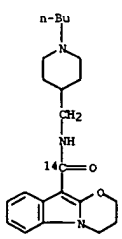
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:549985 CAPLUS
DOCUMENT NUMBER: 134:162978
TITLE: The synthesis of isotopically labeled SB-207266-A
AUTHOR(S): Badman, Geoffrey T.; Mahoney, Alan; Smith, Darren
CORPORATE SOURCE: Synthetic Isotope Chemistry Department, SmithKline Beecham Pharmaceuticals, Harlow, CM19 5AW, UK
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds 1997, Proceedings of the International Symposium, 6th, Philadelphia, PA, United States, Sept. 14-18, 1997 (1998), Meeting Date 1997, 175-178. Editor(s): Heys, J. Richard; Melillo, David G. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69AGFQ
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I

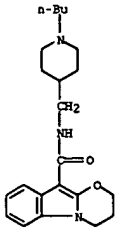
AB A symposium report on the preparation of the title compound (I).
IT **325145-86-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 325145-86-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide-14C, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:466896 CAPLUS
DOCUMENT NUMBER: 133:160168
TITLE: Pharmacological properties of 5-hydroxytryptamine4 receptor antagonists on constitutively active wild-type and mutated receptors
AUTHOR(S): Claeysen, Sylvie; Sebben, Michele; Becamel, Carine; Eglen, Richard M.; Clark, Robin D.; Bockaert, Joel; Dumuis, Aline
CORPORATE SOURCE: Centre National de la Recherche Scientifique Unite Propre de Recherche, Centre National de la Recherche Scientifique-Institut National de la Sante et de la Recherche Medicale de Pharmacologie-Endocrinologie, Montpellier, Fr.
SOURCE: Molecular Pharmacology (2000), 58(1), 136-144
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied the pharmacol. properties of twenty-four 5-hydroxytryptamine (5-HT)4 receptor ligands known to act as antagonists on 5-HT4 receptors pos. coupled to adenylyl cyclase endogenously expressed in mouse colliculi neurons. In COS-7 cells expressing human or mouse 5-HT4(a) receptors (100-8000 fmol/mg of protein), we found neutral antagonists, partial agonists, and inverse agonists. The majority of neutral antagonists belong to the benzodioxanyl ketone class, whereas partial agonists belong to different chemical classes. We found only two inverse agonists, GR 125487 and SB 207266, which are both indoles. Anal. of pharmacol. characteristics of the constitutively active wild-type and constitutively active mutated receptors revealed that (1) the ratio between the efficiencies of the full agonist 5-HT and the partial agonist RS 23597 was invariable when the receptor d. increased, but was dependent on receptor structure; (2) similarly, the efficacy of the inverse agonist SB 207266 was not dependent on receptor d. but was dependent on receptor structure; (3) when the receptor concentration increased, the EC50 values of the full agonist 5-HT were not modified and the increase in basal constitutive activity, as well as its stimulation by 5-HT, followed a parallel evolution; and (4) the stimulation of basal constitutive activity by 5-HT was not modified by the overexpression of Gαs. All these results indicate that in COS-7 cells, the coupling of the 5-HT4 receptor to adenylyl cyclase was linear with no indication of spare receptors even at high receptor d. (8 pmol/mg). These results are also in accordance with a precoupling between the activated receptor (fR*) and adenylyl cyclase. Such observations allowed us to use the two-state model to calculate the constant J, i.e., the equilibrium allosteric constant denoting the ratio of the receptor in the inactive vs. active state (J = [R]/[R*]). We found that J was a receptor structural characteristic, independent of receptor d.
IT 152811-62-6, SB 207266
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT4 receptor antagonist pharmacol. properties on constitutively active wild-type and mutated receptors)
RN 152811-62-6 CAPLUS

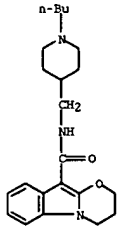
L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:405033 CAPLUS
DOCUMENT NUMBER: 133:115446
TITLE: Increased defecation during stress or after 5-hydroxytryptophan: selective inhibition by the 5-HT4 receptor antagonist, SB-207266
AUTHOR(S): Sanger, G. J.; Yoshida, M.; Yahyah, M.; Kitazumi, K.
CORPORATE SOURCE: Department of Neuroscience Research, SmithKline Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: British Journal of Pharmacology (2000), 130(3), 706-712
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1 5-HT4 receptor antagonism prevents the ability of exogenous 5-HT or 5-HTP to sensitize the intestinal peristaltic reflex and increase the rate of defecation, generally without affecting non-stimulated intestinal function. In this study we confirmed the ability of the selective 5-HT4 receptor antagonist SB-207266 1-1000 μg kg-1 p.o., to prevent the increase in defecation evoked over a 60 min period by 5-HTP 10 mg kg-1 s.c. in conscious mice, in the absence of an apparent constipating action. 2 The role of endogenous 5-HT in the mechanisms of increased defecation and/or diarrhea was then investigated in conscious, fed rats. This was evoked by 180 min exposure to restraint stress, which increased both the number and mean weight of formed, fecal pellets excreted over the entire time period. 3 SB-207266 1-1000 μg kg-1 p.o. (dosed 30 min before restraint) did not affect the increase in defecation evoked during the first 60 min of restraint stress, but significantly and dose-dependently reduced or prevented the increased defecation during the remaining 120 min of the experiment; this action occurred in the absence of an apparent constipating action of SB-207266. 4 In fasted rats exposed to restraint stress, watery diarrhea developed and although there was a tendency for SB-207266 1-1000 μg kg-1 p.o. (dosed 30 min before restraint) to reduce the incidence of diarrhea, this inhibition was not complete. 5 We conclude that selective 5-HT4 receptor antagonism prevents disruptions in defecation behaviors caused by exogenous or endogenous enteric 5-HT and that this activity is not accompanied by a concomitant suppression of activity (constipation-like) within the intestine itself.
IT 152811-62-6, SB-207266
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(increased defecation during stress or after 5-hydroxytryptophan and selective inhibition by 5-HT4 receptor antagonist, SB-207266)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

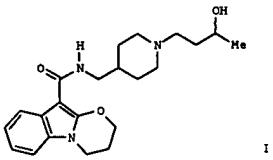


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:210179 CAPLUS
DOCUMENT NUMBER: 132:237100
TITLE: Preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist
INVENTOR(S): Hossner, Frank; Ryan, David Austin
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000017207	A1	20000330	WO 1999-EP6780		19990914
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 2004176370	A1	20040909	US 2004-801510		20040316
PRIORITY APPLN. INFO.:			GB 1998-20294	A	19980917
			WO 1999-EP6780	W	19990914
			US 2002-787980	B1	20020418

GI

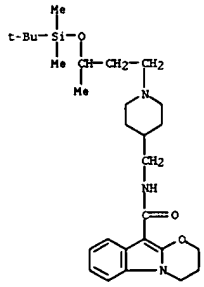


I

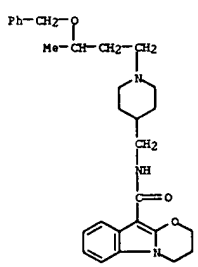
AB The title compound I, useful as 5-HT4 receptor antagonist in the treatment or prophylaxis of gastrointestinal disorders, cardiovascular disorders and CNS disorders, was prepared Compound I was found to have a pKB of 9.3 and did not significantly affect DMPP-evoked contractions of the guinea pig colon.

IT 261787-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist)

L4 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

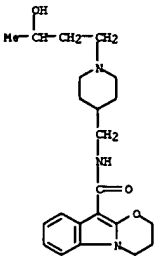


RN 261787-98-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-{[1-[3-(phenylmethoxy)butyl]-4-piperidinyl]methyl}- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl]methyl}- (9CI) (CA INDEX NAME)

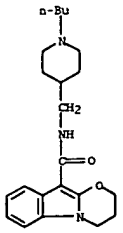


IT 261787-97-7P 261787-98-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist)
RN 261787-97-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]butyl]-4-piperidinyl]methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:786519 CAPLUS
DOCUMENT NUMBER: 132:8863
TITLE: 5-HT4 receptor antagonism in irritable bowel syndrome: effect of SB-207266-A on rectal sensitivity and small bowel transit
AUTHOR(S): Houghton, L. A.; Jackson, N. A.; Whorwell, P. J.; Cooper, S. M.
CORPORATE SOURCE: Department of Medicine, University Hospital of South Manchester, Manchester, M20 2LR, UK
SOURCE: Alimentary Pharmacology and Therapeutics (1999), 13(11), 1437-1444
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Pre-clin. studies indicate that the 5-hydroxytryptamine (5-HT)4 receptor may be involved in the pathophysiol. of irritable bowel syndrome and that antagonism of this receptor may be an effective therapeutic strategy. Aim: To investigate the effects of SB-207266-A, a selective 5-HT4 receptor antagonist on rectal sensitivity and small bowel transit in patients with irritable bowel syndrome. Methods: Eighteen patients with diarrhea-predominant irritable bowel syndrome and a history of increased rectal sensitivity were randomized to receive either SB-207266-A (20 mg) or placebo for 10 days. Following a washout period, patients were then crossed over to receive the alternative therapy for 10 days. Rectal sensitivity and orocaecal transit time were assessed on day 10 of each treatment period. In addition, patients were asked whether they had experienced any changes in their symptoms. Results: Fifteen patients completed the study. SB-207266-A significantly increased orocaecal transit time towards normal (placebo: 5.3 h (4.0-7.2 h), mean (IQR) vs. SB-207266-A: 6.5 h (4.8-8.0 h); P = 0.027) and tended to decrease rectal sensitivity (volume to discomfort 89 mL (60-150 mL), geometric mean (IQR) vs. 107 mL (75-150 mL); P = 0.134). Eleven out of 15 patients reported symptomatic improvements with SB-207266-A but none with placebo. SB-207266-A was well tolerated. Conclusion: Our results support a role for the 5-HT4 receptor in the pathophysiol. of irritable bowel syndrome and suggest that the selective 5-HT4 antagonist, SB-207266-A, is worthy of further evaluation in this disorder.

IT 178273-87-5, SB 207266-A
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of SB-207266-A, 5-HT4 receptor antagonist on rectal sensitivity and small bowel transit in humans with irritable bowel syndrome)
RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl]methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

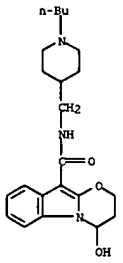
L4 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



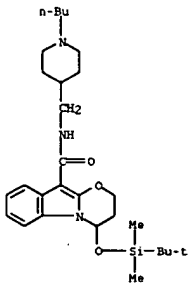
● HCl

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



IT **227328-82-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of an oxazinoindolecarboxamide as a 5-HT4 receptor antagonist)
RN 227328-82-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:388190 CAPLUS
DOCUMENT NUMBER: 131:44832
TITLE: Preparation of an oxazinoindolecarboxamide as a 5-HT4 receptor antagonist
INVENTOR(S): Hoessner, Frank; Fedouloff, Michael; Bush, Brian David
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

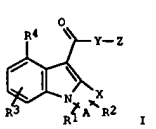
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929697	A1	19990617	WO 1998-EP7764	19981201
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2312844	AA	19990617	CA 1998-2312844	19981201
EP 1037894	A1	20000927	EP 1998-965209	19981201
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001525415	T2	20011211	JP 2000-524290	19981201
US 2001031751	A1	20011018	US 2001-845884	20010430
PRIORITY APPLN. INFO.:			GB 1997-25933 A	19971205
			WO 1998-EP7764 W	19981201
			US 2000-555851 B1	20000713

AB Me indole-3-carboxylate was etherified by HO(CH2)3OH and the cyclized and O-protected product amidated by 1-butyl-4-piperidinemethylamine to give, after deprotection, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-4-hydroxy-2H-[1,3]oxazino[3,2-a]indole-3-carboxamide (I). Data for biol. activity of I were given.
IT **227328-83-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of an oxazinoindolecarboxamide as a 5-HT4 receptor antagonist)
RN 227328-83-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-4-hydroxy- (9CI) (CA INDEX NAME)

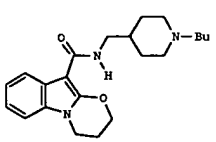
L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:12306 CAPLUS
DOCUMENT NUMBER: 130:81518
TITLE: Preparation of condensed indoles as 5HT4 receptor antagonists
INVENTOR(S): Gaster, Laramie Mary; Wyman, Paul Adrian
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 302,784,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5852014	A	19981222	US 1995-459168	19950602
ZA 9301709	A	19940118	ZA 1993-1709	19930310
EP 884319	A2	19981216	EP 1998-114130	19930310
EP 884319	A3	19990210		
EP 884319	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PRIORITY APPLN. INFO.:			GB 1992-5428 A	19920312
			GB 1992-18846 A	19920905
			GB 1992-27045 A	19921229
			US 1994-302784 B2	19940912
			EP 1993-905561 A3	19930310
OTHER SOURCE(S):	MARPAT 130:81518			

GI



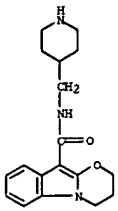
I



II

AB The title compds. [I; X = O, S, SO, etc.; A = (un)saturated polymethylene C2-4 chain; R1, R2 = H, C1-6 alkyl; R3 = H, halo, C1-6 alkyl, etc.; R4 = H, halo, C1-6 alkyl, C1-6 alkoxy; Y = O, NH; Z = (1-n-butyl-4-piperidyl)methyl, 2-(1-piperidyl)ethyl, etc.], useful in the treatment of gastrointestinal disorders, cardiovascular disorders and CNS disorders (e.g. irritable bowel syndrome, urinary incontinence, atrial arrhythmia, and stroke), were prepared Thus, treatment of N-[(1-n-butyl-4-piperidyl)methyl]indole-3-carboxamide with NCS in CHCl3 followed by addition of 3-bromo-1-propanol afforded 17% the title compound II which showed particularly good activity at 5HT4 receptor. Compds. I were generally active as 5-HT4 receptor antagonists in the range of pIC50 ≥ 7.
IT **152811-89-7P 218770-76-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

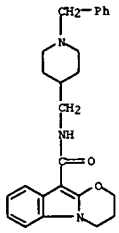
L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
(Reactant or reagent); USES (Uses)
(prepn. of condensed indoles as 5HT4 receptor antagonists)
RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 218770-76-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

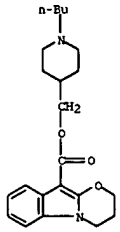
CRN 152811-86-4
CMF C25 H29 N3 O2



CM 2

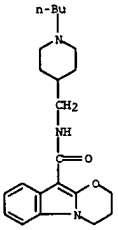
L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CRN 144-62-7
CMF C2 H2 O4

IT 152811-59-1P 152811-62-6P 152811-63-7P
152811-65-9P 152811-67-1P 152811-81-9P
152811-86-4P 152811-90-0P 152811-91-1P
152811-92-2P 152811-94-4P 152811-95-5P
152811-96-6P 152812-01-6P 152812-04-9P
152812-06-1P 162515-59-5P 178273-87-5P
218770-72-0P 218770-74-2P 218770-83-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of condensed indoles as 5HT4 receptor antagonists)
RN 152811-59-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

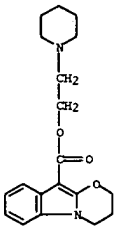


RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

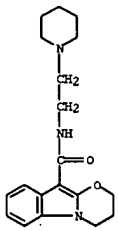


RN 152811-63-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, 2-(1-piperidinyl)ethyl ester (9CI) (CA INDEX NAME)

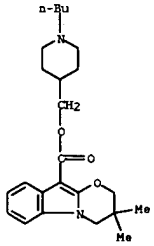


RN 152811-65-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

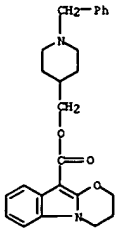


RN 152811-67-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-3,3-dimethyl-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

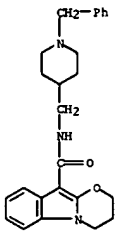


RN 152811-81-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, (1-(phenylmethyl)-4-piperidinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

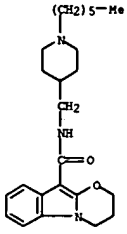


RN 152811-86-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[(1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

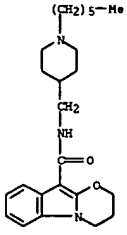


RN 152811-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-hexyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



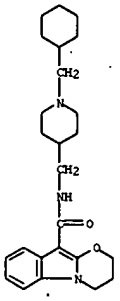
RN 152811-91-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-hexyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



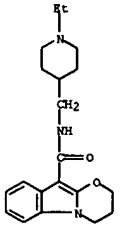
● HCl

RN 152811-92-2 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-(cyclohexylmethyl)-4-piperidinyl]methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

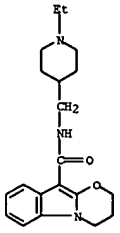


RN 152811-94-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-ethyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



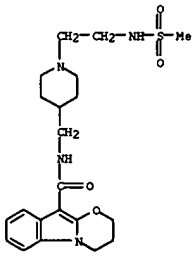
RN 152811-95-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-ethyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



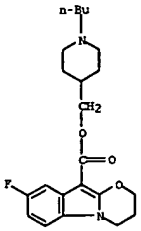
● HCl

RN 152811-96-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-[2-[(methylsulfonyl)amino]ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

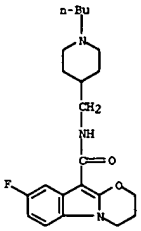


RN 152812-01-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 8-fluoro-3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

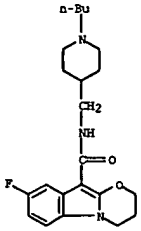


RN 152812-04-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-8-fluoro-3,4-dihydro- (9CI) (CA INDEX NAME)



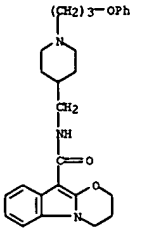
RN 152812-06-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-8-fluoro-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



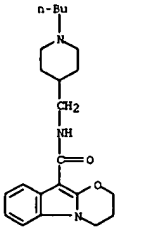
● HCl

RN 162515-59-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-phenoxypropyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



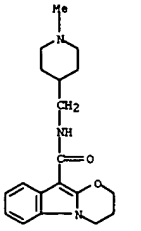
RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 218770-72-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[(1-methyl-4-piperidinyl)methyl]- (9CI) (CA INDEX NAME)

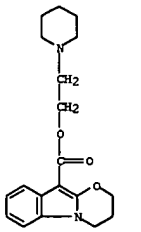


RN 218770-74-2 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, 2-(1-piperidinyl)ethyl ester, ethanedioate (9CI) (CA INDEX NAME)

CM 1

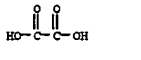
CRN 152811-63-7
CMF C19 H24 N2 O3

L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CM 2

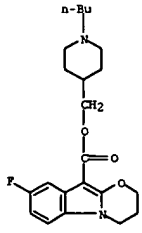
CRN 144-62-7
CMF C2 H2 O4



RN 218770-83-3 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 8-fluoro-3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 152812-01-6
CMF C22 H29 F N2 O3



L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

CM 2

CRN 144-62-7
CMF C2 H2 O4

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

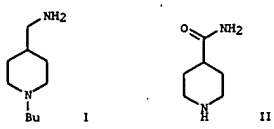
ACCESSION NUMBER: 1998:180842 CAPLUS
DOCUMENT NUMBER: 128:230245
TITLE: Improved preparation of 1-butyl-4-piperidinylmethylamine from isonipecotamide using toluene solvent
INVENTOR(S): Fedouloff, Michael; Guest, David William; Smith, Gillian Elizabeth
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK; Fedouloff, Michael; Guest, David William; Smith, Gillian Elizabeth
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811067	A1	19980319	WO 1997-EP5167	19970909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2266468	AA	19980319	CA 1997-2266468	19970909
AU 9747764	A1	19980402	AU 1997-47764	19970909
AU 725210	B2	20001005		
ZA 9708087	A	19990309	ZA 1997-8087	19970909
EP 927163	A1	19990707	EP 1997-910322	19970909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
BR 9712014	A	19990824	BR 1997-12014	19970909
CN 1230179	A	19990929	CN 1997-197756	19970909
CN 1102927	B	20030312		
NZ 334272	A	20000825	NZ 1997-334272	19970909
JP 2001500148	T2	20010109	JP 1998-513283	19970909
CZ 290932	B6	20021113	CZ 1999-809	19970909
TW 432048	B	20010501	TW 1997-86113072	19970910
NO 9901148	A	19990310	NO 1999-1148	19990310
NO 312587	B1	20020603		
KR 2000038041	A	20000705	KR 1999-701990	19990310
US 6331631	B1	20011218	US 2000-643644	20000822

PRIORITY APPLN. INFO.:
GB 1996-18967 A 19960911
WO 1997-EP5167 W 19970909
US 1999-254513 A1 19990903

OTHER SOURCE(S): CASREACT 128:230245
GI

L4 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

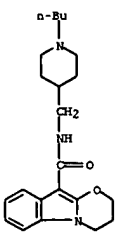


I II

AB An improved process for the preparation of 1-butyl-4-piperidinylmethylamine (I) from isonipecotamide (II) is described. I is an intermediate for the 5-HT4 receptor antagonist SB 207266. The process comprises: (i) reaction of II with BuBr to give the N-Bu derivative, and (ii) reduction with LiAlH4, characterized in that both reactions are carried out in toluene as solvent. The method avoids isolation of intermediates, and uses a single solvent which is free of additives (unlike THF, which contains stabilizers requiring later removal). For instance, II in PhMe was treated with K2CO3 and BuBr at 50° and then refluxed under Dean-Stark conditions. The reaction was quenched with H2O and extracted, and the PhMe layer was dried by azeotropic distillation The PhMe solution was treated with LiAlH4.2THF in PhMe at 5°, followed by stirring at room temperature and then 55°. Alkaline workup and vacuum distillation of the product gave I in 85% yield.

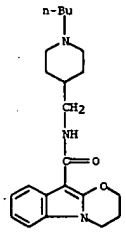
IT 152811-62-6P, SB 207266 178273-87-5P, SB 207266-A
RL: PNU (Preparation, unclassified); PREP (Preparation)
(intermediate for; improved preparation of [(butylpiperidinyl)methyl]amine from isonipecotamide using toluene solvent)

RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

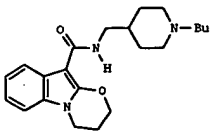
L4 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:147334 CAPLUS
DOCUMENT NUMBER: 128:192660
TITLE: Process for the preparation of N-[(1-n-butyl-4-piperidyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide and salts and intermediates in the process
INVENTOR(S): Fedouloff, Michael; Smith, Gillian Elizabeth; Guest, David William; Strachan, John Bryce
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK; Fedouloff, Michael; Smith, Gillian Elizabeth; Guest, David William; Strachan, John Bryce
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

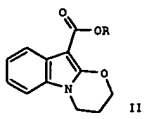
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807728	A1	19980226	WO 1997-EP4413	19970811
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2263480	AA	19980226	CA 1997-2263480	19970811
AU 9742048	A1	19980306	AU 1997-42048	19970811
AU 717177	B2	20000316		
EP 922048	A1	19990616	EP 1997-940076	19970811
EP 922048	B1	20001115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
BR 9711189	A	19990817	BR 1997-11189	19970811
CN 1233250	A	19991027	CN 1997-198712	19970811
CN 1104435	B	20030402		
NZ 334064	A	20000825	NZ 1997-334064	19970811
JP 2000516240	T2	20001205	JP 1998-510360	19970811
AT 197588	E	20001215	AT 1997-940076	19970811
ES 2151743	T3	20010101	ES 1997-940076	19970811
PT 922048	T	20010330	PT 1997-940076	19970811
IL 143230	A1	20020210	IL 1997-143230	19970811
CZ 290517	B6	20020814	CZ 1999-516	19970811
IL 128499	A1	20021110	IL 1997-128499	19970811
PL 185815	B1	20030829	PL 1997-331647	19970811
ZA 9707302	A	19990215	ZA 1997-7302	19970814
TW 427990	B	20010401	TW 1997-86111731	19970815
NO 9900697	A	19990215	NO 1999-697	19990215
NO 311574	B1	20011210		
US 6100397	A	20000808	US 1999-242413	19990216
HK 1020731	A1	20010629	HK 1999-105933	19991216
GR 3034895	T3	20010228	GR 2000-402584	20001122

L4 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
PRIORITY APPLN. INFO.:

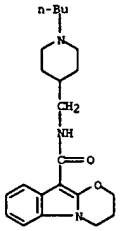
GB 1996-17188	A	19960816
GB 1996-18968	A	19960911
IL 1997-128499	A3	19970811
WO 1997-EP4413	W	19970811
WO 1997-US4413	W	19970811

OTHER SOURCE(S): CASREACT 128:192660; MARPAT 128:192660
GI


I

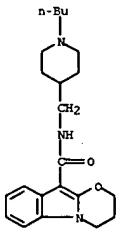

II

AB The title compound SB 207266 (I), having 5-HT4 receptor antagonist activity (no data), was prepared by reaction of 1-n-butyl-4-piperidylmethylamine with the ester II [R = alkyl] in the presence of aluminum or lithium based catalyst such as AlMe3.
IT **152811-62-6P 178273-87-5P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of N-[(1-n-butyl-4-piperidyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide and salts and intermediates in the process)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 178273-87-5 CAPLUS

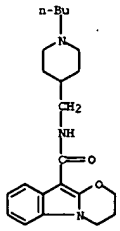
L4 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

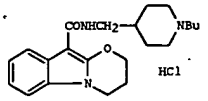
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:128792 CAPLUS
DOCUMENT NUMBER: 128:239261
TITLE: SB-207266: 5-HT4 receptor antagonist agent for irritable bowel syndrome
AUTHOR(S): Gaster, Laramie
CORPORATE SOURCE: Medicinal Chemistry, SmithKline Beecham, New Frontiers Science Park, Essex, CM19 5AW, UK
SOURCE: Drugs of the Future (1997), 22(12), 1325-1332
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: J. R. Prous, S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Selective 5-HT4 receptor antagonists offer a new approach for the treatment of functional gastrointestinal disorders, acting to remove a cause of hypersensitivity without affecting the normal function of the gut. A pilot study with SB-207266 in patients with irritable bowel syndrome (IBS) now strongly supports the involvement of 5-HT in the mechanisms of IBS and suggests a key role for 5-HT4 receptor antagonism in the future management of this disorder.
IT **152811-62-6P, SB 207266**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(SB-207266 as 5-HT4 receptor antagonist for treatment of irritable bowel syndrome)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:430878 CAPLUS
DOCUMENT NUMBER: 127:145052
TITLE: Anxiolytic-like actions of the selective 5-HT4 receptor antagonists SB 204070A and SB 207266A in rats
AUTHOR(S): Kennett, G. A.; Bright, F.; Trail, B.; Blackburn, T. P.; Sanger, G. J.
CORPORATE SOURCE: Psychiatry Research, SmithKline Beecham Pharmaceuticals, Harlow, CM19 5AW, UK
SOURCE: Neuropharmacology (1997), 36(4/5), 707-712
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



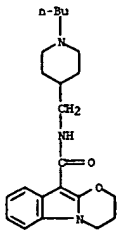
I

AB The highly selective 5-HT4 receptor antagonists, SB 204070A (0.001-0.1 mg/kg s.c., 30 min pre-test) and SB 207266A (I) (0.01, 1 and 10 mg/kg p.o., 1 h pre-test), increased time spent in social interaction without affecting locomotor activity, in a rat 15 min social interaction test under high light, unfamiliar conditions. At 1 and 10 mg/kg s.c., SB 204070A was no longer active. These results are consistent with the profile expected of anxiolytic treatments in this procedure. In a rat 5 min elevated x-maze test, SB 204070A (0.01 and 1 mg/kg s.c., 30 min pre-test) significantly increased the percentage of time spent on the open arms. SB 204070A (0.01 mg/kg s.c.) and SB 207266A (1 mg/kg p.o., 1 h pre-test) also increased percentage entries to the open arms. Neither compound affected locomotion at any dose tested in the procedure. The effects of both compds. in this procedure are also consistent with anxiolysis. Neither SB 204070A (0.1 or 1 mg/kg s.c., 30 min pre-test) nor SB 207266A (0.1 or 1 mg/kg p.o., 1 h pre-test) affected either unpunished or punished responding, in a rat Geller-Seifter conflict model of anxiety. The maximal efficacy of both SB 204070A and SB 207266A in the rat social interaction test was similar to that of the benzodiazepine anxiolytic chlordiazepoxide (5 mg/kg s.c. or p.o.) used as a pos. control, but was considerably less in the elevated x-maze procedure. The results suggest that 5-HT4 receptor antagonists may have modest anxiolytic-like actions in rats.

IT 178273-87-5, SB 207266A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anxiolytic-like actions of the selective 5-HT4 receptor antagonists SB 204070A and SB 207266A in rats)

RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-

L4 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

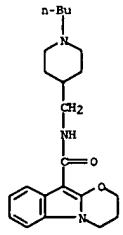
L4 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:365145 CAPLUS
DOCUMENT NUMBER: 125:48902
TITLE: Selective and functional 5-hydroxytryptamine4 receptor antagonism by SB 207266
AUTHOR(S): Wardle, K. A.; Bingham, S.; Ellis, E. S.; Gaster, L. M.; Rushant, B.; Smith, M. I.; Sanger, G. J.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: British Journal of Pharmacology (1996), 118(3), 665-670
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacol. of a novel 5-HT4 receptor antagonist, SB 207266 has been evaluated in vitro in the guinea-pig distal colon longitudinal muscle myenteric plexus (LMMP) and in vivo in the dog Heidenhain pouch. SB 207266 is a highly potent antagonist of 5-HT-evoked, cholinergically-mediated contractions in the guinea-pig distal colon. Low concns. (0.1-10 nM) produced a parallel shift to the right of the concentration-effect curve (apparent pA2 10.6) with no significant effect on the maximum response. With higher concns. of SB 207266 (30 nM and above) the maximum response to 5-HT was reduced. The antagonism seen with SB 207266 cannot be attributed to a non-selective effect since high concns. (1 μM) had no effect on cholinergically-mediated contractions evoked by the nicotinic receptor agonist DMPP in the same preparation. SB 207266 is not an irreversible antagonist since the effects of the compound were reversible upon washing of the tissue. In the dog Heidenhain pouch, oral (0.1-100 μg kg-1) and i.v. (0.1-100 μg kg-1) administration of SB 207266 produced a dose-dependent antagonism of the contractions evoked by a bolus i.v. injection of 5-HT. An ID50 for SB 297266 of 1.3 μg kg-1 was obtained following i.v. administration and 9.6 μg kg-1 following oral administration. The antagonistic effects of SB 207266 (0.1 μg kg-1) in the dog Heidenhain pouch were long lasting since, following oral administration, the response to 5-HT was reduced for at least 135 min. SB 207266 is a highly potent, highly selective and orally active 5-HT4 receptor antagonist. This compound is the first orally active amide to be identified in this class of antagonists and as such is an important new tool in the evaluation of 5-HT4 receptor function both in vitro an in vivo.

IT 178273-87-5, SB 207266
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(selective and functional 5-hydroxytryptamine4 receptor antagonism by SB 207266)

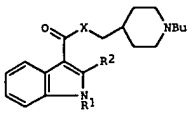
RN 178273-87-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

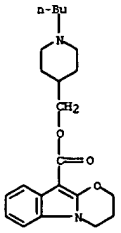
L4 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:905955 CAPLUS
DOCUMENT NUMBER: 124:117202
TITLE: N-[(1-Butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole- 10-carboxamide hydrochloride: the first potent and selective 5-HT4 receptor antagonist amide with oral activity.
AUTHOR(S): Gaster, Laramie M.; Joiner, Graham F.; King, Frank D.; Wyman, Paul A.; Sutton, Jonathan M.; Bingham, Sharon; Ellis, Elizabeth S.; Sanger, Gareth J.; Wardle, Kay A.
CORPORATE SOURCE: New Frontiers Science Park, SmithKline Beecham Pharmaceuticals, Harlow Essex, CM19 5AW, UK
SOURCE: Journal of Medicinal Chemistry (1995), 38(24), 4760-3
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



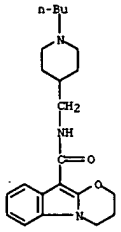
I

AB SB 207266A, [I; R1R2 = (CH2)3O; X = NH] (II) (preparation from indole-3-carboxylic acid given), is a potent, selective, and orally active 5-HT4 receptor antagonist which shows >1000-fold selectivity for the 5-HT4 receptor compared with affinities for 5-HT1A, 5-HT1D, 5-HT1E, 5-HT2A, 5-HT2C, 5-HT3, dopamine D2 and D3 and histamine H1 receptors. II in the guinea pig distal colon LMMP assay antagonized 5-HT evoked contractions with pIC50 = 9.2, and at 100 μg/kg i.v. in dogs in a Heidenhain gastric pouch assay caused virtually complete abolition of contractile response to 5-HT.
IT **152811-59-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of (butylpiperidinylmethyl)indolecarboxamide derivs. as 5-HT4 antagonists)
RN 152811-59-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



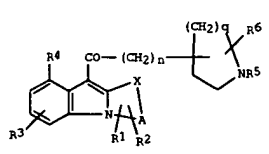
IT **152811-62-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (butylpiperidinylmethyl)indolecarboxamide derivs. as 5-HT4 antagonists)
RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:508085 CAPLUS
DOCUMENT NUMBER: 122:265390
TITLE: Preparation of condensed indole derivatives as 5-HT4 receptor antagonists.
INVENTOR(S): Gaster, Laramie Mary; Wyman, Paul Adrian
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9504737	A1	19950216	WO 1994-EP2514	19940728
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2168750	AA	19950216	CA 1994-2168750	19940728
AU 9476098	A1	19950228	AU 1994-76098	19940728
AU 695034	B2	19980806		
EP 712406	A1	19960522	EP 1994-926128	19940728
EP 712406	B1	19981028		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1131949	A	19960925	CN 1994-193556	19940728
JP 09502168	T2	19970304	JP 1994-506201	19940728
AT 172732	E	19981115	AT 1994-926128	19940728
ES 2125481	T3	19990301	ES 1994-926128	19940728
ZA 9405773	A	19960205	ZA 1994-5773	19940803
TW 396158	B	20000701	TW 1994-83107151	19940804
US 5998409	A	19991207	US 1995-459934	19950602
HK 1012347	A1	20000512	HK 1998-113455	19981215
PRIORITY APPLN. INFO.:			GB 1993-16195 A	19930805
			GB 1992-5428 A	19920312
			GB 1992-18846 A	19920905
			GB 1992-27045 A	19921229
			WO 1994-EP2514 W	19940728

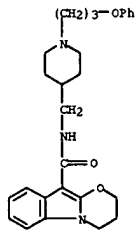
OTHER SOURCE(S): MARPAT 122:265390
GI



I

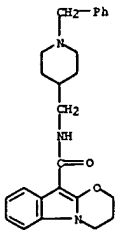
AB Title compds. [I; X = O, S, SO, SO2, CH2, CH, NR; R = H, C1-6 alkyl; A = (unsatd.) C2-4 polymethylene; R1, R2 = H, C1-6 alkyl; R3 = H, halo, C1-6 alkyl, amino, NO2, C1-6 alkyl; R4 = H, halo, C1-6 alkyl, C1-6 alkoxy; Y = O, NH; n = 1-4; q = 0-3; R5 = 3-phenoxypropyl; R6 = H, alkyl; COY = heterocyclic bioisostere], were prepd. Thus, N-(4-piperidinylmethyl)-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide (prepn. given), Et3N, and 3-phenoxypropyl bromide were refluxed in DMF/MeCN to give N-[(1-(3-phenoxypropyl)-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide. The latter showed pIC50 = 9.65 in a test for 5-HT4 receptor antagonist activity in guinea pig colon.
IT **162515-59-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of condensed indole derivs. as 5-HT4 receptor antagonists)
RN 162515-59-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-phenoxypropyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

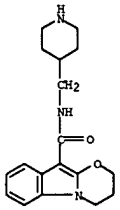


IT **152811-86-4P 152811-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of condensed indole derivs. as 5-HT4 receptor antagonists)
RN 152811-86-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

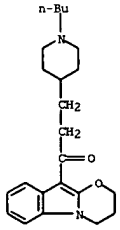
L4 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



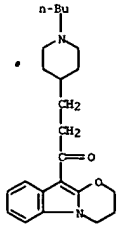
L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 1-Propanone, 3-(1-butyl-4-piperidinyl)-1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)- (9CI) (CA INDEX NAME)



RN 161680-14-4 CAPLUS
CN 1-Propanone, 3-(1-butyl-4-piperidinyl)-1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 161680-13-3
CMF C23 H32 N2 O2



CM 2

CRN 144-62-7
CMF C2 H2 O4

L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:428909 CAPLUS
DOCUMENT NUMBER: 122:187597
TITLE: Preparation of heterocyclic 5-HT4 receptor antagonists
INVENTOR(S): King, David Francis; Gaster, Laramie Mary; Mulholland, Keith Raymond
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427987	A1	19941208	WO 1994-EP1583	19940516
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2163372	AA	19941208	CA 1994-2163372	19940516
AU 9469283	A1	19941220	AU 1994-69283	19940516
AU 693449	B2	19980702		
EP 699194	A1	19960306	EP 1994-917637	19940516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1126472	A	19960710	CN 1994-192690	19940516
JP 08510266	T2	19961029	JP 1995-500169	19940516
ZA 9403493	A	19951120	ZA 1994-3493	19940520
US 5741801	A	19980421	US 1995-553390	19951122
US 5872134	A	19990216	US 1998-13138	19980126
US 6114329	A	20000905	US 1998-13385	19980126
US 2002019386	A1	20020214	US 2001-939914	20010827
US 2003139389	A1	20030724	US 2002-317159	20021211

PRIORITY APPLN. INFO.:

GB 1993-10582	A	19930522
WO 1994-EP1583	W	19940516
US 1995-553390	A3	19951122
US 1998-13135	B1	19980126
US 2001-939914	B1	20010827

OTHER SOURCE(S): MARPAT 122:187597

AB The title compds. XCOCH2Z [X = (un)substituted benzoheterocyclyl, (un)substituted Ph, (un)substituted naphthyl, (un)substituted heterocyclyl; Z = (un)substituted heterocyclyl, (un)substituted pyridopyridinyl, (un)substituted aminoalkyl], useful as 5-HT4 receptor antagonists in the treatment of gastrointestinal disorders, cardiovascular disorders, and CNS disorders, are prepared Thus, 1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)-3-(1-butyl-4-piperidinyl)propan-1-one oxalate salt (m.p. 156-159°) was prepared from pyridine-4-carboxaldehyde in 4 steps.

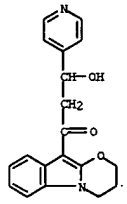
IT **161680-13-3P 161680-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic 5-HT4 receptor antagonists)

RN 161680-13-3 CAPLUS

L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

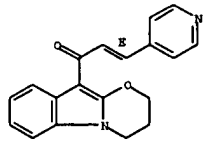
IT **161680-10-0P 161680-11-1P 161680-12-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic 5-HT4 receptor antagonists)

RN 161680-10-0 CAPLUS
CN 1-Propanone, 1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)-3-hydroxy-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)



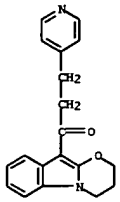
RN 161680-11-1 CAPLUS
CN 2-Propen-1-one, 1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)-3-(4-pyridinyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 161680-12-2 CAPLUS
CN 1-Propanone, 1-(3,4-dihydro-2H-[1,3]oxazino[3,2-a]indol-10-yl)-3-(4-pyridinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:557655 CAPLUS
DOCUMENT NUMBER: 121:157655
TITLE: Piperidine derivative 5-HT4 receptor antagonists
INVENTOR(S): Gaster, Laramie Mary; Wyman, Paul Adrian
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9410174	A1	19940511	WO 1993-EP3054	19931102
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2148700	AA	19940511	CA 1993-2148700	19931102
AU 9454197	A1	19940524	AU 1994-54197	19931102
AU 680453	B2	19970731		
EP 667867	A1	19950823	EP 1993-924569	19931102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502741	T2	19960326	JP 1993-510716	19931102
ZA 9308204	A	19940819	ZA 1993-8204	19931103
CN 1092422	A	19940921	CN 1993-112680	19931104
US 5705498	A	19980106	US 1995-433369	19950504

PRIORITY APPLN. INFO.:
GB 1992-23155 A 19921105
GB 1993-9644 A 19930511
GB 1993-15202 A 19930722
WO 1993-EP3054 W 19931102

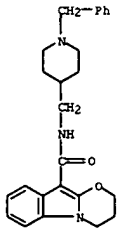
OTHER SOURCE(S): MARPAT 121:157655

AB The title compds. XCOYZ {X = (un)substituted monocyclic or polycyclic aromatic group; Y = O, NH; Z = (un)substituted N-containing (alkyl)heterocyclyl residue}, useful as 5-HT4 receptor antagonists (no data) for the treatment or prophylaxis of gastrointestinal diorders (no data), cardiovascular diorders (no data), and CNS disorders (no data), are prepared Thus, 8-amino-7-chloro-1,4-benzodioxan-5-(4-piperidinylmethyl)carboxylate was condensed with 3-picolyl chloride and salified with oxalic acid, producing 5-[1-(3-pyridiylmethyl)-4-piperidinyl]methyl-8-amino-7-chloro-1,4-benzodioxancarbonxylate oxalate, m.p. 219-221°.

IT **152811-86-4P 152811-88-6P 152811-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of 5-HT4 receptor antagonists)

RN 152811-86-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

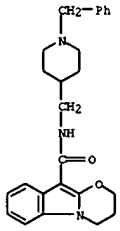
L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152811-88-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 152811-86-4
CMF C25 H29 N3 O2

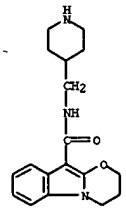


CM 2

CRN 144-62-7
CMF C2 H2 O4

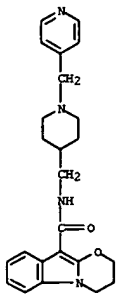
L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)



IT **157330-66-0P 157330-67-1P 157330-68-2P**
157330-69-3P 157330-70-6P 157330-71-7P
157330-72-8P 157330-73-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT4 receptor antagonist)

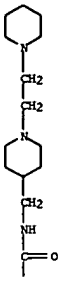
RN 157330-66-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(4-pyridinylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



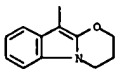
RN 157330-67-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-[2-(1-piperidinyl)ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



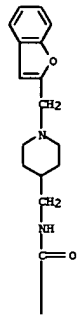
PAGE 2-A



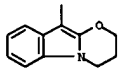
RN 157330-68-2 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-(2-benzofuranylmethyl)-4-piperidinyl]methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



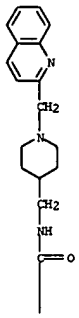
PAGE 2-A



RN 157330-69-3 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(2-quinolinylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A



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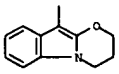
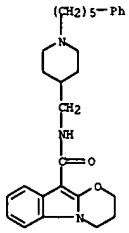
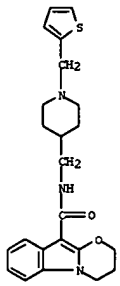


RN 157330-70-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(5-phenylpentyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



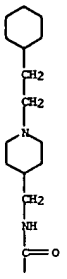
RN 157330-71-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(2-thienylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



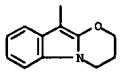
RN 157330-72-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-(2-cyclohexylethyl)-4-piperidinyl]methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

PAGE 1-A

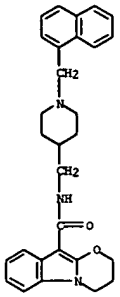


PAGE 2-A



RN 157330-73-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(1-naphthalenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN

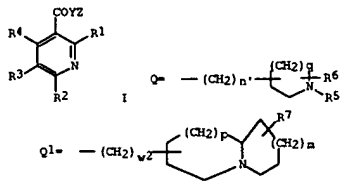
ACCESSION NUMBER: 1994:557530 CAPLUS
DOCUMENT NUMBER: 121:157530
TITLE: Preparation of substituted pyridine 5-HT4 antagonists
INVENTOR(S): King, Francis David; Gaster, Laramie Mary; Wyman, Paul Adrian; Joiner, Graham Francis
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407859	A1	19940414	WO 1993-GB2028	19930928
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9348305	A1	19940426	AU 1993-48305	19930928
CN 1092766	A	19940928	CN 1993-114190	19930928
ZA 9307183	A	19950118	ZA 1993-7183	19930928
EP 662959	A1	19950719	EP 1993-921024	19930928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502056	T2	19960305	JP 1993-508839	19930928
US 5696129	A	19971209	US 1995-406951	19950329

PRIORITY APPLN. INFO.:

GB 1992-20508	A	19920929
GB 1992-21774	A	19921016
GB 1992-21791	A	19921016
GB 1992-23135	A	19921105
GB 1992-23138	A	19921105
GB 1992-24604	A	19921124
GB 1993-9642	A	19930511
GB 1993-11878	A	19930609
WO 1993-GB2028	W	19930928

OTHER SOURCE(S): MARPAT 121:157530
GI



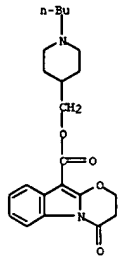
AB Title compds. I (R1= C1-6 alkoxy; R2 = H, C1-6 alkyl, substituted amino; R3 = H, halo, C1-6 alkyl, C1-6 alkoxy, O2N, H2N, C1-6 alkylthio; R4 = H,

L4 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

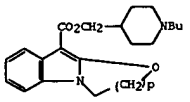
halo, C1-6 alkyl, C1-6 alkoxy, H2N, (substituted)7-azaindolyl, (substituted) pyridinyl, (substituted) heterocyclyl; Y = O, HN; Z = Q, Q1, R8R9N(CH2)n3 wherein R5 = H, C1-12 alkyl, aralkyl, etc., R6-8 = H, C1-6 alkyl, R9 = H, C1-10 alkyl, n1, n2 = 0-4, n3 = 2-5, m, p = 0-2, q = 0-3) and a salt thereof, are prepd. I had a pIC50 (-log conc.of antagonist which reduces the contraction by 50%) of at least 7. I are claimed for use in treatment of gastrointestinal disorders, cardiovascular disorders and CNS disorders. I (R1 = MeO, R2 = H2N, R3 = Cl, R4 = Z = H, Y = O) (prepn. given) in MeCN was heated to 40° and the residue obtained was added to (2-hydroxyethyl)piperidine Li salt to give I (R1 = MeO, R2 = H2N, R3 = Cl, R4 = H, Y = O, Z = 1-ethylpiperidinyl).

IT 156270-25-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT4 antagonist)

RN 156270-25-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-4-oxo-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

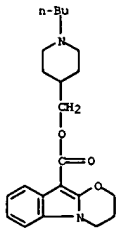


L4 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:449603 CAPLUS
DOCUMENT NUMBER: 121:49603
TITLE: 5-HT4 receptor antagonists: oxazolo, oxazino and oxazepino[3,2-a]indole derivatives
AUTHOR(S): Gaster, L. M.; Wyman, P. A.; Ellis, E. S.; Young, T. J.
CORPORATE SOURCE: SmithKline Beecham Pharm., Harlow/Essex, CM19 5AD, UK
SOURCE: Bioorg. Med. Chem. Lett. (1994), 4(5), 667-8
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The identification of oxazolo, oxazino and oxazepino[3,2-a]indoles as new structural classes of highly potent 5-HT4 receptor antagonists is described. Compds. I (p = 1, 2, 3) are among the most potent 5-HT4 receptor antagonists reported to date.
IT 152811-59-1
RL: BIOL (Biological study)
(serotoninergic S4 antagonist, structure in relation to)
RN 152811-59-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

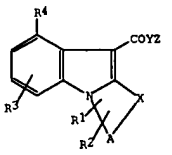
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:134454 CAPLUS
DOCUMENT NUMBER: 120:134454
TITLE: Condensed indole derivatives as 5HT4-receptor antagonists
INVENTOR(S): Gaster, Laramie Mary; Wyman, Paul Adrian
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318036	A1	19930916	WO 1993-GB506	19930310
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9336448	A1	19931005	AU 1993-36448	19930310
AU 671102	B2	19960815		
ZA 9301709	A	19940118	ZA 1993-1709	19930310
EP 630376	A1	19941228	EP 1993-905561	19930310
EP 630376	B1	19990602		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07504433	T2	19950518	JP 1993-515490	19930310
JP 2831467	B2	19981202		
HU 71121	A2	19951128	HU 1994-2601	19930310
HU 219121	B	20010228		
IL 105003	A1	19960912	IL 1993-105003	19930310
PL 172692	B1	19971128	PL 1993-305013	19930310
RU 2104279	C1	19980210	RU 1994-40864	19930310
EP 884319	A2	19981216	EP 1998-114130	19930310
EP 884319	A3	19990210		
EP 884319	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 180785	E	19990615	AT 1993-905561	19930310
ES 2132223	T3	19990816	ES 1993-905561	19930310
CZ 286194	B6	20000216	CZ 1994-2210	19930310
SK 281423	B6	20010312	SK 1994-1078	19930310
AT 266033	E	20040515	AT 1998-114130	19930310
PT 884319	T	20040930	PT 1998-114130	19930310
ES 2219813	T3	20041201	ES 1998-114130	19930310
CN 1043893	B	19990630	CN 1993-102648	19930311
NO 9403348	A	19941109	NO 1994-3348	19940909
NO 303638	B1	19980810		
FI 9404204	A	19940912	FI 1994-4204	19940912
FI 107158	B1	20010615		
HK 1012352	A1	20000623	HK 1998-113467	19981215

PRIORITY APPLN. INFO.:
GB 1992-5428 A 19920312
GB 1992-18846 A 19920905
GB 1992-27045 A 19921229
EP 1993-905561 A3 19930310
WO 1993-GB506 A 19930310

OTHER SOURCE(S): MARPAT 120:134454
GI

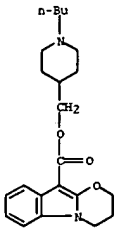
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



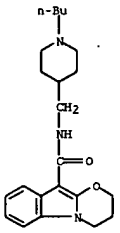
I

AB The title compds. I [A = (un)saturated C2-4 polymethylene chain; R1, R2 = H, C1-6 alkyl; R3 = H, halogen, C1-6 alkyl, amino, nitro, C1-6 alkoxy; R4 = H, halogen, C1-6 alkyl, C1-6 alkoxy; X = O, S, SO, SO2, CH2, CH, (un)substituted NH; Y = O, NH; Z = (un)substituted heterocyclylalkyl, aminoalkyl], useful as a serotonin T4 receptor antagonists (no data) for the treatment or prophylaxis of gastrointestinal disorders (no data), cardiovascular disorders (no data), and CNS disorders (no data), are prepared Thus, indole-3-carboxylic acid was converted to its acid chloride, esterified with 1-butyl-4-piperidinemethanol, the ester treated with N-chlorosuccinimide and 3-bromo-1-propanol, producing (1-butyl-4-piperidyl)methyl-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxylate, m.p. 117-119°.
IT 152811-59-1P 152811-62-6P 152811-63-7P
152811-64-8P 152811-65-9P 152811-67-1P
152811-81-9P 152811-86-4P 152811-88-6P
152811-90-0P 152811-91-1P 152811-92-2P
152811-93-3P 152811-94-4P 152811-95-5P
152811-96-6P 152811-97-7P 152812-01-6P
152812-03-8P 152812-04-9P 152812-06-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and serotonin receptor antagonist activity of)
RN 152811-59-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

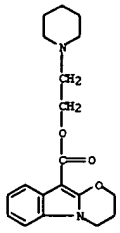


RN 152811-62-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 152811-63-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, 2-(1-piperidinyl)ethyl ester (9CI) (CA INDEX NAME)

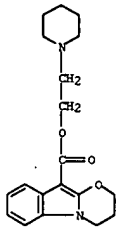
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152811-64-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, 2-(1-piperidinyl)ethyl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 152811-63-7
CMF C19 H24 N2 O3

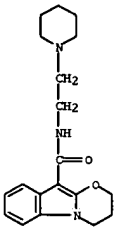


CM 2

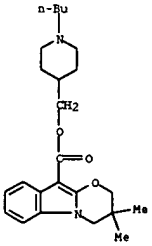
CRN 144-62-7
CMF C2 H2 O4

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 152811-65-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

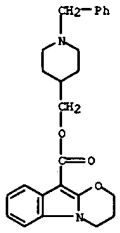


RN 152811-67-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-3,3-dimethyl-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)

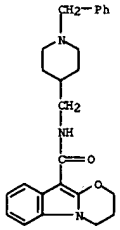


RN 152811-81-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 3,4-dihydro-, [1-(phenylmethyl)-4-piperidinyl]methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152811-86-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

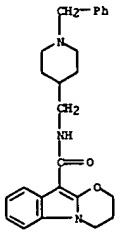


RN 152811-88-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 152811-86-4
CMF C25 H29 N3 O2

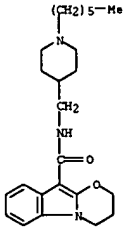
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



CM 2

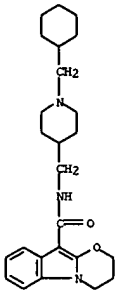
CRN 144-62-7
CMF C2 H2 O4

RN 152811-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-hexyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



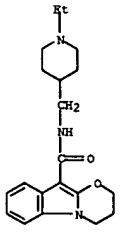
RN 152811-91-1 CAPLUS

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-(cyclohexylmethyl)-4-piperidinyl]methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



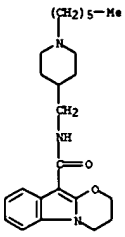
● HCl

RN 152811-94-4 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-ethyl-4-piperidinyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



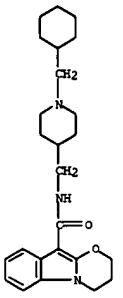
RN 152811-95-5 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-ethyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-hexyl-4-piperidinyl)methyl]-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



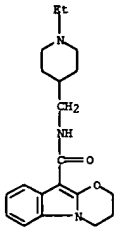
● HCl

RN 152811-92-2 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[[1-(cyclohexylmethyl)-4-piperidinyl]methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



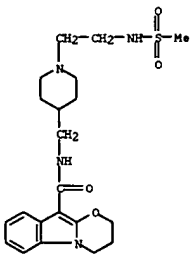
RN 152811-93-3 CAPLUS

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

RN 152811-96-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-[2-[(methylsulfonyl)amino]ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 152811-97-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-[2-[(methylsulfonyl)amino]ethyl]-4-piperidinyl]methyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

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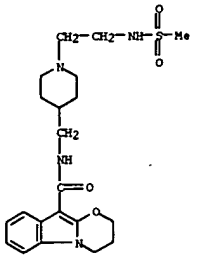
CRN 152811-96-6
CMF C21 H30 N4 O4 S

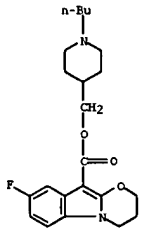
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



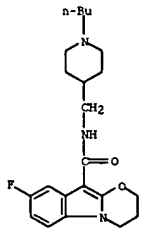
CM 2

CRN 144-62-7
CMF C2 H2 O4

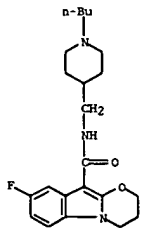
RN 152812-01-6 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 8-fluoro-3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 152812-06-1 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-8-fluoro-3,4-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

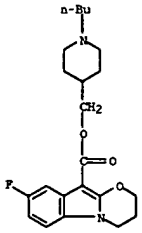
IT 152811-89-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and serotonin receptor antagonist activity of, reaction of)
RN 152811-89-7 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-(4-piperidinylmethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RN 152812-03-8 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxylic acid, 8-fluoro-3,4-dihydro-, (1-butyl-4-piperidinyl)methyl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 152812-01-6
CMF C22 H29 F N2 O3

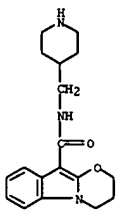


CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 152812-04-9 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, N-[(1-butyl-4-piperidinyl)methyl]-8-fluoro-3,4-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



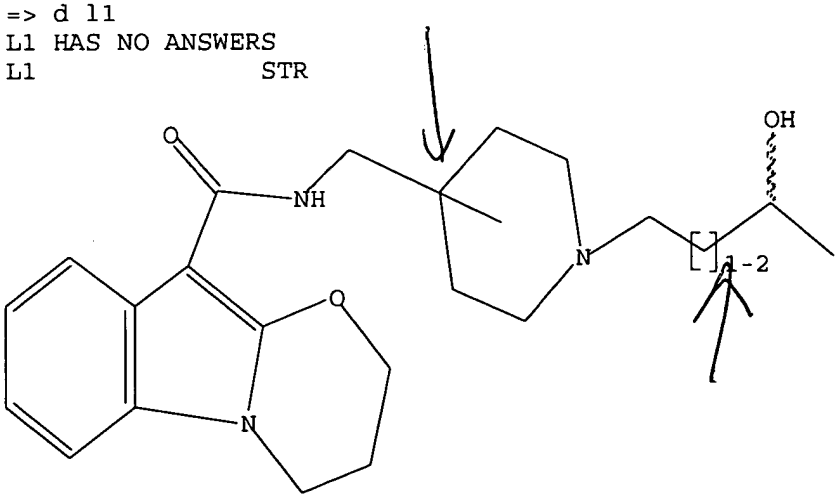
Broad search (2)

chain nodes :
14 15 16 17 24 25 26 27 28
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 18 19 20 21 22 23
chain bonds :
7-14 14-15 14-16 16-17 21-24 24-25 25-26 26-27 26-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-13 7-8 8-13 8-9 9-10 10-11 11-12 12-13
18-23 18-19 19-20 20-21 21-22 22-23
exact/norm bonds :
5-7 6-13 7-8 8-13 8-9 9-10 10-11 11-12 12-13 14-15 14-16 16-17 18-23
18-19 19-20 20-21 21-22 21-24 22-23 26-28
exact bonds :
7-14 24-25 25-26 26-27
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

<03/09/2005> Habte

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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 08:10:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      5 TO ITERATE

100.0% PROCESSED       5 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

L3            1 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 161.33     161.54

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FILE COVERS 1907 - 9 Mar 2005  VOL 142 ISS 11
FILE LAST UPDATED: 8 Mar 2005  (20050308/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            2 L3

=> d ibib abs hitstr tot
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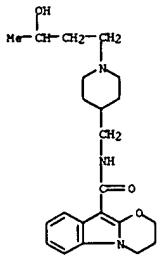
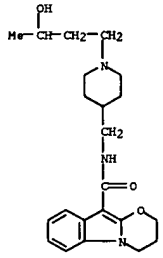
L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:591194 CAPLUS
DOCUMENT NUMBER: 135:344435
TITLE: Synthesis and pharmacological activity of metabolites of the 5-HT4 receptor antagonist SB-207266
AUTHOR(S): Fedculoff, M.; Hossner, F.; Voyle, M.; Ranson, J.; Powles, J.; Riley, G.; Sanger, G.
CORPORATE SOURCE: Department of Synthetic Chemistry, Smithkline Beecham Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(8), 2119-2128
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344435
AB Three metabolites of N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]-oxazino[3,2-a]indole-10-carboxamide (SB-207266) were synthesized and their pharmacol. activity determined
IT 261787-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of metabolites of 5-HT4 receptor antagonist SB-207266)
RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-hydroxybutyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-hydroxybutyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:210179 CAPLUS
DOCUMENT NUMBER: 132:237100
TITLE: Preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist
INVENTOR(S): Hossner, Frank; Ryan, David Austin
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017207	A1	20000330	WO 1999-EP6780	19990914
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2004176370	A1	20040909	US 2004-801510	20040316
PRIORITY APPLN. INFO.:			GB 1998-20294	A 19980917
			WO 1999-EP6780	W 19990914
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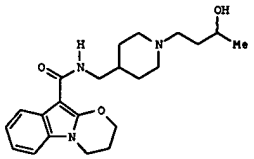
GI



I

AB The title compound I, useful as 5-HT4 receptor antagonist in the treatment or prophylaxis of gastrointestinal disorders, cardiovascular disorders and CNS disorders, was prepared Compound I was found to have a pKB of 9.3 and did not significantly affect DMPP-evoked contractions of the guinea pig colon.
IT 261787-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist)

(1)

chain nodes :
14 15 16 17 24 25 26 27 28
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 18 19 20 21 22 23
chain bonds :
7-14 14-15 14-16 16-17 17-18 21-24 24-25 25-26 26-27 26-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-13 7-8 8-13 8-9 9-10 10-11 11-12 12-13
18-19 18-23 19-20 20-21 21-22 22-23
exact/norm bonds :
5-7 6-13 7-8 8-13 8-9 9-10 10-11 11-12 12-13 14-15 14-16 16-17 18-19
18-23 19-20 20-21 21-22 21-24 22-23 26-28
exact bonds :
7-14 17-18 24-25 25-26 26-27
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS

L1 STRUCTURE UPLOADED

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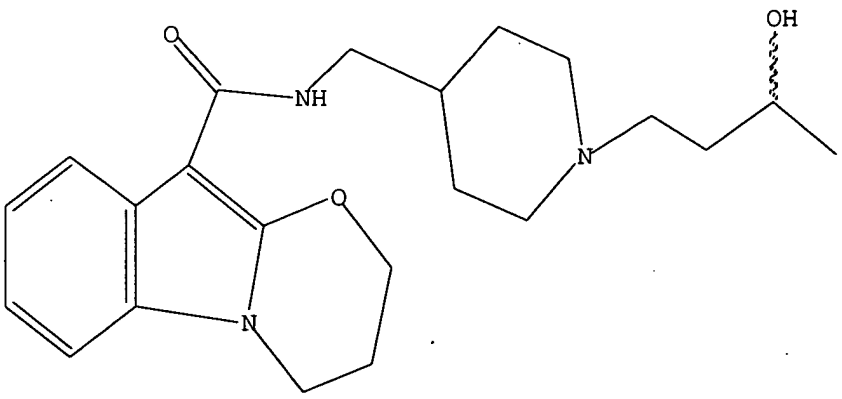
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

<03/09/2005> Habte

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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             0 TO         0
PROJECTED ANSWERS:                0 TO         0

L2            0 SEA SSS SAM L1

=> s l1 sss full
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FULL SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

L3            1 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                161.33     161.54

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FILE COVERS 1907 - 9 Mar 2005  VOL 142 ISS 11
FILE LAST UPDATED: 8 Mar 2005  (20050308/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            2 L3

=> d ibib abs hitstr tot
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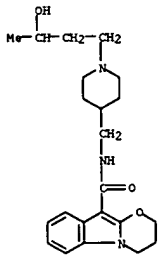
own work

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:591194 CAPLUS
DOCUMENT NUMBER: 135:344435
TITLE: Synthesis and pharmacological activity of metabolites of the 5-HT4 receptor antagonist SB-207266
AUTHOR(S): Fedouloff, M.; Hossner, F.; Voyle, M.; Ranson, J.; Powles, J.; Riley, G.; Sanger, G.
CORPORATE SOURCE: Department of Synthetic Chemistry, Smithkline Beecham Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(8), 2119-2128
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:344435

AB Three metabolites of N-[(1-butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]-oxazino[3,2-a]indole-10-carboxamide (SB-207266) were synthesized and their pharmacol. activity determined

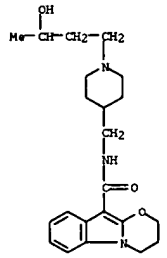
IT 261787-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and pharmacol. activity of metabolites of 5-HT4 receptor antagonist SB-207266)

RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-hydroxybutyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RN 261787-90-0 CAPLUS
CN 2H-[1,3]Oxazino[3,2-a]indole-10-carboxamide, 3,4-dihydro-N-[[1-(3-hydroxybutyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

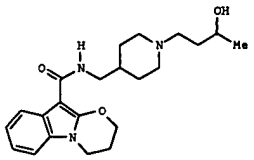


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:210179 CAPLUS
DOCUMENT NUMBER: 132:237100
TITLE: Preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist
INVENTOR(S): Hossner, Frank; Ryan, David Austin
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017207	A1	20000330	WO 1999-EP6780	19990914
W: CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2004176370	A1	20040909	US 2004-801510	20040316
PRIORITY APPLN. INFO.:			GB 1998-20294	A 19980917
			WO 1999-EP6780	W 19990914
			US 2002-787980	B1 20020418

GI



I

AB The title compound I, useful as 5-HT4 receptor antagonist in the treatment or prophylaxis of gastrointestinal disorders, cardiovascular disorders and CNS disorders, was prepared Compound I was found to have a pKB of 9.3 and did not significantly affect DMPP-evoked contractions of the guinea pig colon.

IT 261787-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,4-dihydro-N-{[1-(3-hydroxybutyl)-4-piperidinyl] methyl}-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide as 5-HT4 receptor antagonist)